III. REMARKS

The final Office Action dated November 9, 2006, has been received and carefully noted. The above amendments and the following remarks are being submitted as a full and complete response thereto.

Claims 1-27 are pending in the application. Claims 8-18 and 20-25 are withdrawn. By this Amendment, claims 1, 2, 4, 6, and 26 are amended. The amendments are supported by the originally filed specification and claims. In particular, the amendments to claim 1 are supported, for example, by page 5, lines 12-30 and page 3, lines 14-21 of the specification. No new matter is added.

Entry of this Amendment is proper under 37 C.F.R. §1.116 since this Amendment: (a) places the application in condition for allowance for reasons discussed herein; (b) does not raise any new issue regarding further search and/or consideration since the Amendment amplifies issues previously discussed throughout prosecution; (c) does not present any additional claims without canceling a corresponding number of finally-rejected claims; and (d) places the application in better form for appeal, should an appeal be necessary. Entry of the Amendment is thus respectfully requested.

Claims 1-7, 19, and 26-27 are rejected under 35 U.S.C. § 112, first paragraph, for insufficient written description. This rejection is traversed.

Applicants respectfully submit that this rejection has been overcome by the above amendments to the claims 1, 2, 4, 6, and 26 which removes the letter "Z", as suggested by the Examiner on page 3, line 5 of the Office Action, which was made in order to expedite prosecution.

Applicants respectfully submit that the "genetically engineered live attenuated Newcastle disease virus" of the present claims is sufficiently described by the specification. Applicants had possession of the system to manipulate the genome of Newcastle disease virus (NDV) at the time of the original filing of this application. Genetically engineered live attenuated Newcastle disease virus could be engineered from a strain of NDV with the modifications clearly described in claims 1-7, 19, and/or 26-27.

As also previously noted, this application discloses creative engineering of a recombinant live attenuated NDV vaccine that will be more genetically stable than currently-available natural vaccine strains. For example, the specification notes that "the ability to directly engineer mutations into cDNA would make it possible to generate defined attenuated strains where cDNA would serve as a stable vaccine 'seed'" (specification, page 3, lines 15-17).

Thus, for at least the above reasons, Applicants submit that the present specification and the claims provide sufficient written description for "genetically engineered live attenuated Newcastle disease virus." Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-7, 19 and 26-27 under 35 U.S.C. § 112, first paragraph.

Claims 1-3, 5, 15, and 19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Millar et al. (Journal of General Virology (1998) 69: 613-620). This rejection is traversed.

Present claim 1 is directed to "[a] vaccine for Newcastle disease comprising a genetically engineered live attenuated Newcastle disease virus, wherein the genetically engineered live attenuated Newcastle disease virus has a F_o protein cleavage site having at least two less basic amino acid residues than a F_o protein cleavage site of Newcastle disease virus wild type strain Beaudette C, wherein codons of at least two non-basic amino acid residues replacing the at least two basic amino acid residues are different from codons of the basic amino acid residues by at least two nucleotides; and at least one of the features selected from the group consisting of: (1) an amino acid having a non-aromatic side chain at the N terminus of the F_1 cleavage fragment, wherein the amino acid having a nonaromatic side chain is glycine, alanine, valine, leucine or isoleucine; and (2) an open reading frame of a HN glycoprotein being longer than an open reading frame of a HN glycoprotein of Newcastle disease virus wild type strain Beaudette C, wherein the genetically engineered live attenuated disease virus is in the form of a vaccine for administration to a subject" (emphasis added).

Applicants respectfully maintain that Millar et al. does not anticipate present claim 1, as Millar et al. does not teach or suggest a vaccine, much less a vaccine of the genetically engineered live attenuated Newcastle disease virus of present claim 1.

Further, Millar et al. does not teach or suggest the genetically engineered live attenuated Newcastle disease virus of present claim 1 with "a F_o protein cleavage site having at least two less basic amino acid residues than a F_o protein cleavage site of Newcastle disease virus wild type strain Beaudette C" and "wherein codons of at least two non-basic amino acid residues replacing the at least two basic amino acid residues

are different from codons of the basic amino acid residues by at least two nucleotides." As such, if two basic amino acid residues at the F_o protein cleavage site are replaced with two non-basic amino acid residues, each of the codons of the two new non-basic amino acid residues will differ from the codons of the replaced basic amino acid residues by at least two nucleotides. If more than two basic amino acid residues are replaced with non-basic amino acid residues, the codons of at least two of the new non-basic amino residues will differ from the codons of the replaced basic amino acid residues by at least two nucleotides.

In contrast, as previously noted, Millar et al. discloses that

> ... There were fewer basic amino acids at the cleavage site of F_0 in strain Ulster than are present in more virulent strains, which may be responsible for the absence of cleavage and activation of F_0 from this strain in many host cells.

(Millar et al., Abstract) (emphasis added). Accordingly, Millar et al. merely discloses a lesser amount of basic amino acids with a potential correlation to virulence. Millar et al. does not teach or suggest a difference of "at least two nucleotides" in the codons of at least two non-basic amino acids replacing the basic amino acids at the F_o protein cleavage site as in present claim 1, much less the unexpected stability of the presently claimed invention. Those of skill in the art would understand that a change from a basic amino acid to a non-basic amino acid does not require a difference of at least two nucleotides.

For example, the present specification discloses that "a difference in at least two nucleotides stabilizes the viral genome against reversion from a nonbasic amino acid residue to a basic amino acid residue" (specification, page 5, lines 13-15). Further, the

specification discloses that the "genetically engineered NDV strains of the present invention are completely apathogenic and will not revert back to virulence phenotypes" and that "[t]hese new NDV strains are better than the currently available NDV vaccines" (specification, page 5, lines 27-30).

Applicants respectfully submit that the claims are directed to a product, i.e., a vaccine, and not a product-by-process as asserted in the paragraph bridging page 3 of the Office Action. Please see, for example, present claim 1. As noted above, the genetically engineered live attenuated Newcastle disease virus of presently claimed invention is distinguishable as Millar et al. does not teach or suggest a difference of "at least two nucleotides" in the codons of at least two non-basic amino acids replacing the basic amino acids at the F_o protein cleavage site of the genetically engineered live attenuated Newcastle disease virus of the vaccine of present claim 1. Further, even if the claims were improperly considered to be product-by-process claims, the product is distinguishable based upon the unexpected stability of the genetically engineered live attenuated Newcastle disease virus of the vaccine of the presently claimed invention.

Applicants also respectfully submit that a definition of the phrase "genetically engineered live attenuated" in the specification is not necessary as those of skill in the art would clearly have understood the meanings of such terms. As noted by the Examiner, "[t]he definition of attenuated is 'less virulent or weakened'" (Office Action, page 3, second full paragraph). Meanwhile, "genetically engineered" is generally defined, for example, as "the directed alteration of genetic material by intervention in genetic processes," and "live" is generally defined, for example, as having life. See the

two attached webpages from Webster's Third New International Dictionary Unabridged, available at http:///mwu.eb.com/mwu.

As Millar et al. does not teach or suggest all of the elements of the present claim 1, Applicants submit that Millar et al. does not anticipate present claim 1. Dependent claims 2-3, 5, 15, and 19 are not anticipated for at least the same reasons. Accordingly, for at least the above reasons. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-3, 5, 15, and 19 under 35 U.S.C. § 102(b) as being anticipated by Millar et al.

Claims 4 and 6-7 are rejected under 35 U.S.C. § 103(a) as being unpatentable over by Millar et al. (Journal of General Virology (1998) 69: 613-620) in view of Peeters et al. (WO 99/66045). This rejection is traversed.

Applicants submit that dependent claims 4 and 6-7 are patentable for at least the same reasons as claim 1. Please see the above discussion distinguishing Millar et al. from present claim 1.

In particular, Applicants respectfully maintain that Peeters et al. does not satisfy the deficiencies of Millar et al. For example, as noted by the Examiner, Peeters et al. discloses the following:

> Furthermore, a method is provided to modify an avian-paramyxovirus genome by means of genetic modification which allows the introduction of one or more mutations, deletions, and/or insertions or other modifications. For example, method is provided to attenuate or modify the virulence of avian paramyxovirus by modif[y]ing cDNA ... and cloning said modified cDNA into full-length cDNA and generating infectious copy virus from said full-length cDNA, thereby generating new NDV strains or new attenuated live vaccines with improved properties.

(Peeters et al., page 8, lines 23-33) (emphasis added);

> The process can be used to modify the virulence of NDV, thereby generating new attenuated live vaccines with enhanced properties.

(Peeters et al., Abstract) (emphasis added). However, Applicants respectfully submit that Peeters et al. does not teach or suggest "at least two less basic amino acid residues than a F_o protein cleavage site of Newcastle disease virus wild type strain Beaudette C, wherein codons of at least two non-basic amino acid residues replacing the at least two basic amino acid residues are different from codons of the basic amino acid residues by at least two nucleotides" as in present claim 1 (emphasis added), much less the unexpected stability of the presently claimed invention.

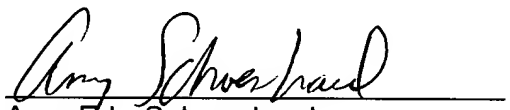
Therefore, as neither Millar et al. nor Peeters et al. teach or suggest every element of the present claim 1, Applicants respectfully submit that present claim 1 would not have been obvious to those of skill in the art in view of Millar et al. and Peeters et al. Dependent claims 4 and 6-7 are patentable for at least the same reasons as claim 1. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 4 and 6-7 under 35 U.S.C. § 103(a) as being unpatentable over Millar et al. and Peeters et al.

III. Conclusion

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

In the event that this paper is not considered to be timely filed, an appropriate extension of time is requested. Any fees for such an extension, together with any additional fees that may be due with respect to this paper, may be charged to counsel's Deposit Account Number 01-2300, referencing Docket Number **108172-00070**.

Respectfully submitted,



Amy E.L. Schoenhard
Registration No. 46,512

Customer No. **004372**
ARENT FOX LLP
1050 Connecticut Avenue, N.W., Suite 400
Washington, D.C. 20036-5339
Tel: (202) 857-6000
Fax: (202) 857-6395

Enclosures: Petition for Extension of Time (one month)
webpages (2)

Main Entry: **genetic engineering**
Function: noun

: the directed alteration of genetic material by intervention in genetic processes; *especially* : GENE-SPLICING *herein*
- **genetically engineered** *adjective*
- **genetic engineer** *noun*

To cite:
"genetic engineering" *Merriam-Webster's Third New International Dictionary Unabridged*
<http://mwu.eb.com/mwu>
[Accessed February 22, 2007].

Main Entry: ^{2}**live**
Pronunciation: 'lIv
Function: adjective
Inflected Form: -er/-est
Etymology: short for *alive*

1 : having life : LIVING <she purged a *live* eel -- Robert Burton> <ships *live* cattle>
2 : abounding with life : VITAL, VIVID <the portrait is ... always *live* and spirited -- *Times Literary Supplement*> <a *live* appreciation of the role of cultural forces in history -- L.A.White> <he saw an oldening, flaccid face with *live* eyes -- Maurice Walsh>
3 : exerting force or containing energy: as **a** : AFIRE, GLOWING <tossed a *live* cigarette from the car> **b** : connected to electric power <a thousand-volt wire, *live* and burning with its power -- Adria Langley> **c** : charged with explosives and containing shot or a bullet <a *live* shell> <a *live* cartridge> <*live* ammunition>; *also* : UNDISCHARGED, UNEXPLODED <a *live* bomb> **d** : imparting or driven by power : having motion <the *live* center of a lathe> <*live* conveyor rolls> **e** : charged with fissionable material <the pile was built up ... with alternating layers of *live* and dead blocks -- L.R.Hafstad>
4 : living in thought or controversy : of continuing interest : open to debate : not settled or decided : UNCLOSED <long-standing denominational disputes still were *live* issues -- Oscar Handlin>
5 : being in a pure native state: as **a** *of a mineral* : NATIVE, VIRGIN **b** *of rock* : UNWROUGHT, UNQUARRIED
6 a : of bright vivid color **b** : of normal brightness or luster -- used of timber and lumber
7 : highly reverberant -- used of a room or enclosed space in which sound is produced; compare ANECHOIC, DEAD 10
8 a *of a playing card* : available for play because still in the hands or stock **b** : being in play <a *live* ball>
9 *of rubber* : SPRINGY, RESILIENT
10 a : not yet printed from or plated : to be held for possible further or future printing -- used of a printing surface **b** : not yet typeset; *also* : typeset but not yet proofread **c** : used for storing or holding live matter
11 a : of or relating to a performance done without mechanical reproduction by phonograph or cinema : presented directly by musicians or actors in concert hall or theater or on radio or television : not recorded or filmed **b** : present and responsive -- used of a radio or television studio audience